UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,084	12/01/2006	Robert L. Wolfert	DEX0478US.NP	4146

32800 7590 05/26/2010

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
05/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,084	WOLFERT ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,16,18-21,24,25,30-32 and 36-39* is/are pending in the application.

4a) Of the above claim(s) *3,8,9,16,18-21,24,25,30-32,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2,4-7,10-11,36,39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants arguments and amendments filed 3/2/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Applicant's previously elected with traverse Group II (claims 1-11,16,18-21) and the following species:

Variable/s measured: Lp-PLA2 and CRP

Patient disorder/patient population: hypertension

In the instant case the elected species were found in the prior art. As such the examination is limited to the generic claims and claims to the elected species in accord with section 803.02 of the MPEP. In the instant case, claim 1 is the only claim that reads on hypertension as claims 18-21,37-38 for example read on a different subset of patients. In the instant case, claims 3,8-9,16 for example read on measuring LDL a non-elected species. Claims 24-25,30-32 are drawn to a different group.

Claims 24-25,30-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/08.

Claims 3,8-9,16,18-21,37-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/08.

Although applicants request rejoinder of claims, no generic claim is allowable.

Claims 12-15,17,22-23,26-29,33-35 have been cancelled.

Claims 1-2,4-7,10-11,36,39 are under consideration.

Claim Rejections - 35 USC § 102

Claims were previously rejected under 102 based on the reference cited below. The rejection is maintained. Since the claims have been amended, the rejection is updated. Since applicants arguments are drawn to both the 102 and 103 rejections such arguments are addressed after the 103 rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2,4-7,11,36,39 are rejected under 35 U.S.C. 102(b) as being anticipated by Packard et al. (NEJM Oct 19 2000 v343 pages 1148-1155; cited with office action 4/15/08).

Packard teach that there are reports that C-reactive protein (CRP) levels are elevated in those at risk for coronary disease (page 1148 column 2 1st paragraph). Packard teach that lipoprotein-associated phospholipase A2 (Lp-PLA2, also known as platelet-activating factor acetylhydrolase) is a potential predictor of the risk of coronary heart disease (page 1148 column

2 2nd paragraph). Packard confirms that CRP and Lp-PLA2 are indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Thus the specific disease recited in claims 2,36 of the instant invention is met. Packard teach that the patient population includes patients with hypertension (table 1) thus meeting the limitation of the elected patient population. Packard teach that CRP and Lp-PLA2 were measured in aliquots of plasma collected from patients (page 1149 'measurements' section 2nd paragraph) thus the sampling (which is a step of the measuring process) was done simultaneously thus meeting the limitations of claim 4 of the instant invention and the samples were from patients as recited in claim 39. Packard also teach that separate enzyme-linked immunoassays were performed for CRP and Lp-PLA2 (page 1149 'measurements' section 2nd and 3rd paragraphs) thus the assaying (which is a step of the measuring process) was performed sequentially thus meeting the limitations of claim 5 of the instant invention. Packard teach that Lp-PLA2 mass was measured (page 1149 'measurements' section 3rd paragraph) thus meeting the limitation of claim 11 of the instant invention. Packard teach that quintile ranges (i.e. divided into 5 classes) were established for the variables (page 1149 'statistical analysis' section 1st paragraph). Since there are 5 classes there are necessarily high and low levels as well as high, medium, and low levels as recited in claims 6-7 of the instant invention. It is noted that claims 6-7 recite 'and a patient having both high CRP and high Lp-PLA2 levels is indicative of heightened risk of CVD'. However, such recitation does not require steps to be performed and do not limit the claim scope (see MPEP section 2111.04). Packard specifically teach a multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. combine the risks in the model). Packard confirms that CRP and Lp-PLA2 are both indicators of risk of coronary heart

disease (page 1152 'discussion' section 1st paragraph). Taken together, Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 'measurements' section 2nd paragraph), analyzing the risks (Table 5), and combining the risks (page 1152 'discussion' section 1st paragraph, Table 5) thus meeting the limitations of claim 1 of the instant invention.

Claim Rejections - 35 USC § 103

Claims were previously rejected under 103 based on the reference cited below. The rejection is maintained. Since the claims have been amended, the rejection is updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2,4-7,10-11,36,39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Packard et al. (NEJM Oct 19 2000 v343 pages 1148-1155; cited with office action 4/15/08) and further in view of Rao et al. (US 2003/0120134; cited with office action 4/15/08).

As discussed above Packard teach that there are reports that C-reactive protein (CRP) levels are elevated in those at risk for coronary disease (page 1148 column 2 1st paragraph). Packard teach that lipoprotein-associated phospholipase A2 (Lp-PLA2, also known as platelet-activating factor acetylhydrolase) is a potential predictor of the risk of coronary heart disease (page 1148 column 2 2nd paragraph). Packard confirms that CRP and Lp-PLA2 are indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Thus the specific disease recited in claims 2,36 of the instant invention is met. Packard teach that the patient population includes patients with hypertension (table 1) thus meeting the limitation of the elected patient population. Packard teach that CRP and Lp-PLA2 were measured in aliquots of plasma collected from patients (page 1149 'measurements' section 2nd paragraph) thus the sampling (which is a step of the measuring process) was done simultaneously thus meeting the limitations of claim 4 of the instant invention and the samples were from patients as recited in claim 39. Packard also teach that separate enzyme-linked immunoassays were performed for CRP and Lp-PLA2 (page 1149 'measurements' section 2nd and 3rd paragraphs) thus the assaying (which is a step of the measuring process) was performed sequentially thus meeting the limitations of claim 5 of the instant invention. Packard teach that Lp-PLA2 mass was measured (page 1149 'measurements' section 3rd paragraph) thus meeting the limitation of claim 11 of the instant invention. Packard teach that quintile ranges (i.e. divided into 5 classes) were established for the variables (page 1140 'statistical analysis' section 1st paragraph). Since there are 5 classes there

are necessarily high and low levels as well as high, medium, and low levels as recited in claims 6-7 of the instant invention. It is noted that claims 6-7 recite 'and a patient having both high CRP and high Lp-PLA2 levels is indicative of heightened risk of CVD'. However, such recitation does not require steps to be performed and do not limit the claim scope (see MPEP section 2111.04). Packard specifically teach a multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. combine the risks in the model). Packard confirms that CRP and Lp-PLA2 are both indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Taken together, Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 'measurements' section 2nd paragraph), analyzing the risks (Table 5), and combining the risks (page 1152 'discussion' section 1st paragraph, Table 5) thus meeting the limitations of claim 1 of the instant invention.

Packard does not expressly teach the use of ATP III guidelines as recited in claim 10.

Rao et al. teach systems and methods for screening for coronary heart disease (abstract). Rao teach that patients are assessed for risk for coronary heart disease based on factors (section 0032). Rao specifically teach that the Adult Treatment Panel (ATP III) has produced guidelines for risk. Rao teach the use of the guidelines in the system for screening for coronary heart disease.

Both Packard and Rao teach methods for assessing risk of coronary heart disease. Since there is evidence that cardiovascular risk and disease is under-treated (Rao section 0005) one would be motivated to use various methods and combinations of methods to assess risk of

coronary heart disease. In particular one would be motivated to use the CRP and Lp-PLA2 risks and additionally use the ATP III guidelines as taught by Rao with the method of Packard thus meeting the limitations of the claims of the instant invention. It is noted that it is obvious to combine compositions each of which is taught by the prior art to be useful for the same purpose (see MPEP section 2144.06). Likewise is it obvious to combine risks (such as those associated with CRP, Lp-PLA2, and ATP III guidelines) for the purpose of assessing the risk of coronary heart disease.

In the instant case all the claimed elements were known in the art as discussed above and one skilled in the art could have combined the elements by known methods and the combination would have yielded predictable results. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments

Applicants argue (pages 10-16) that Packard does not teach combining into one risk and that the markers were not combined.

Applicants argue that Packard makes reference to assessment of the independence of the variables and that the models used by Packard do not report risks of CVD.

Applicants argue that the risks are the output of the model used by Packard.

Applicants argue that the terms in the claims are to be given the broadest reasonable interpretation but the art is not be interpreted so broadly as to draw conclusions not drawn by the authors themselves.

Applicants argue that the previously submitted declaration pertains to differences between the reference and the instant invention.

Applicants argue that the claims have been amended and that Packard does not teach combining the risks.

Applicants argue that Packard uses multivariate models to assess the independent value of variables.

Applicants argue that other references to not remedy the deficiencies.

Applicant's arguments filed 3/2/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 10-16) that Packard does not teach combining into one risk and that the markers were not combined, it is noted that the features upon which applicant relies (i.e., 'one risk') are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims recite 'combine the risks' (not 'one risk'). The caption of Table 5 of Packard states 'Model 2 included the variables in model 1 as well as the traditional risk factors shown'. Table 5 shows the risk factors CRP and Lp-PLA2. Since the model included such variables (the title of the table recites multivariate assessment) the risks were combined as claimed.

Although Applicants argue that Packard makes reference to assessment of the independence of the variables and that the models used by Packard do not report risks of CVD, it is noted that what is concluded from an experiment is separate and distinct from what method steps are carried out. As discussed above Packard teach the active steps (i.e. measure, analyze, combine) of instant claim 1 thus the limitations of claim 1 are met. Table 5 is entitled 'Multivariate assessment of the effect of inflammatory markers on the risk of a coronary event'. Thus one would recognize that the model assesses the risk of a coronary event. No special definition is provided for the word 'combine' in the instant specification, thus the term is given the broadest reasonable interpretation. Further, no special definition is provided for the word 'assess'. Thus the term is given the broadest reasonable interpretation. Table 5 is entitled 'Multivariate assessment of the effect of inflammatory markers on the risk of a coronary event'. As such, the model uses a combination of variables, including Lp-PLA2 and CRP to assess the risk. Packard confirms that CRP and Lp-PLA2 are indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Thus the specific disease recited in claims 2,36 of the instant invention is met. On page 11 of the reply applicants state: "the models used by Packard do not report risks of CVD, only the independence of variables within the model to individually and independently assess risk of CVD". Such argument is unclear since applicants argue that Packard 'do not report risks of CVD', yet 'assess risk of CVD'. Further, applicants state (page 11-12 connecting sentence) that the risks are the output of the model. By definition, to assess is to determine a value. Thus, based on applicants arguments the risks are assessed. It is noted that the instant claims active steps are measure, analyze, and combine which is taught by the prior art. Further, Packard expressly teach assessment of risk (Table 5).

Although Applicants argue that the terms in the claims are to be given the broadest reasonable interpretation but the art is not be interpreted so broadly as to draw conclusions not drawn by the authors themselves, it is noted that the instant claims are not drawn to methods of drawing conclusions. As discussed above Packard teach the active steps (i.e. measure, analyze, combine) of instant claim 1 thus the limitations of claim 1 are met. What is concluded from the data is not the relevant issue since conclusions are an unclaimed feature.

Although Applicants argue that the previously submitted declaration pertains to differences between the reference and the instant invention, Section 706.02(b) of the MPEP lists ways of overcoming a 102(b) rejection. However, submission of a declaration is not listed as a way to overcome a 102(b) rejection. Thus the declaration is not sufficient to overcome the 102(b) rejection. With regard to the 103 rejection, it appears that the declaration is opinion evidence (see MPEP section 716.01(c)). Section 716.01(c) of the MPEP states that the opinion as to a legal conclusion is not entitled to any weight. Although applicants argue that there are differences in the references, it is noted that a reference does not have to be identically worded to be anticipatory (see MPEP 2131). As discussed above Packard teach the active steps (i.e. measure, analyze, combine) of instant claim 1 thus the limitations of claim 1 are met. As discussed previously (see office action 9/2/09), applicants declaration filed 4/17/09 has been fully considered but is not persuasive.

Although Applicants argue that the claims have been amended and that Packard does not teach combining the risks, the caption of Table 5 of Packard states 'Model 2 included the variables in model 1 as well as the traditional risk factors shown'. Table 5 shows the risk factors CRP and Lp-PLA2. Since the model included such variables (the title of the table recites

multivariate assessment) the risks were combined as claimed. It is noted that the phrase 'combining the risks' does not give any specifics on how the risks were combined.

Although Applicants argue that Packard uses multivariate models to assess the independent value of variables, the title of Table 5 expressly recites 'multivariate assessment' and 'risk of a coronary event'. Multivariate by definition means have more than one variable. What is concluded from an experiment is separate and distinct from what method steps are carried out. As discussed above Packard teach the active steps (i.e. measure, analyze, combine) of instant claim 1 thus the limitations of claim 1 are met.

Although Applicants argue that other references to not remedy the deficiencies, such argument is not sufficient to overcome the outstanding 102 or 103 rejections.

Relevant Prior Art

The prior art previously made of record and not relied upon is considered pertinent to applicant's disclosure:

Dada and Kim and Wolfert, (Expert Rev Mol Diagn, Jan 2002, 2(1) starts on page 17 abstract only, 2 pages; retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11963798?ordinalpos=12&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum on 8/6/09).

Caslake et al (Atherosclerosis 150 (2000) pages 413-419).

Dada teach that there is accumulating evidence that Lp-PLA2 is a potential biomarker of coronary heart disease (abstract).

Caslake also teach that Lp-PLA2 is a potential new risk factor for coronary heart disease. Thus the teachings of the prior art suggest the use of Lp-PLA2 is a risk marker (abstract).

Conclusion

Claims were previously rejected under 102 based on the reference cited below. The rejection is maintained. Since the claims have been amended, the rejection is updated. Claims were previously rejected under 103 based on the reference cited below. The rejection is maintained. Since the claims have been amended, the rejection is updated.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-

3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654